

SUBSTITUTE FORM PTO-1390 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER 06501-080001
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If Known, see 37 CFR 1.5) <div style="font-size: 1.5em; font-weight: bold;">09/831591</div>
INTERNATIONAL APPLICATION NO. PCT/JP99/04520	INTERNATIONAL FILING DATE 23 August 1999	PRIORITY DATE CLAIMED 13 November 1998
TITLE OF INVENTION HYBRIDIZATION PROBE		
APPLICANT(S) FOR DO/EO/US Tomoyasu Sugiyama, Toshio Ota, Shizuko Ishii and Ai Wakamatsu		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input checked="" type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)). 4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input checked="" type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). 7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input checked="" type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 		
Items 11 to 16 below concern other documents or information included:		
<ol style="list-style-type: none"> 11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> A change of power of attorney and/or address letter. 16. <input type="checkbox"/> Other items or information: <div style="margin-left: 20px;"> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> </div> 		

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DESCRIPTION

HYBRIDIZATION PROBE5 Technical Field

The present invention relates to a labeled DNA and a method for detecting genes with the labeled DNA.

Background Art

10 Labeled DNAs have been utilized in a wide variety of analytical methods based on the specific interaction between DNAs having complementary nucleotide sequences. The following DNA-labeling methods are known:

15 (1) a method in which a radioisotope-labeled phosphate group is introduced into the 5' end of synthetic DNA with T4 polynucleotide kinase;

(2) a method in which biotin or digoxigenin is directly added to the end of oligo DNA by a chemical method, thereby labeling the DNA; or

20 (3) a method in which a labeled nucleotide is added to an oligo DNA with terminal transferase or the like after the DNA is synthesized.

However, it is difficult to prepare probes having high specific activity by the method (1) or (2) of these methods. Only one label molecule per DNA molecule can be introduced by the methods, because
25 the label is linked to only an end of the DNA molecule according to the methods. Therefore, high specific activity cannot be expected based on the methods.

On the other hand, multiple nucleotides are connected together in the method of (3), which is also referred to as 3'-tailing label
30 method. A number of labeled nucleotides or nucleotide derivatives (hereafter, the term "nucleotide compounds", which means both nucleotides and nucleotide derivatives, is used in some cases) can be introduced into a DNA and can achieve high specific activity. It is sometimes difficult to introduce multiple nucleotide derivatives
35 by this method because of steric hindrance by the nucleotide derivatives to be introduced. However, the problem of steric